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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,689	06/29/2007	Ryan Smith Westberry	186257/US	9609

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,689	WESTBERRY ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 15-18* is/are rejected.

7)☒ Claim(s) *13 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/23/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The IDS received on April 23, 2008 is proper and is being considered by the Examiner.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because some of the Figures are not legible. For example, Figure 2, contains tables of reagents and their concentration which are so small that they are not readily legible. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 13 and 14 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claims. See MPEP § 608.01(n). Accordingly, the claims 13 and 14 not been further treated on the merits.

Claim 14 is objected to for the following minor informalities:

Claim 14 recites the phrase, "further comprising at least one additional unconventional nucleotide, wherein the combined concentration said dUTP..." It would appear that there should be the word, "of" between the word, "concentration," and the word, "said."

Correction is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 recite the limitation, "the primer pair."

There is insufficient antecedent basis for this limitation in the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method reducing primer aggregation during an amplification a target nucleic acid, wherein said target nucleic acid is DNA, does not reasonably provide enablement for the method, wherein said target nucleic acid is RNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in In Re Wands (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

Amount of Direction & Guidance – Enablement Issues:

The instant specification clearly states that "conventional nucleotide refers to a nucleotide which naturally occur in a particular nucleic acid," (page 5, lines 21-22), describing that ATP, TTP, CTP, and GTP are considered "conventional" when that particular nucleic acid is DNA.

The instant specification further states that "unconventional nucleotide refers to a nucleotide that is not naturally occurring in a particular nucleic acid," (page 5, lines 25-26), describing that uracil, while naturally occurring in RNA (or particular nucleic acid), could be "unconventional" when the particular nucleic acid in question is DNA (page 5, lines 29-30).

Claims 11 and 12 are drawn to a method of reducing primer aggregation/amplifying nucleic acids, wherein the method involves amplification of a target nucleic acid with a reaction mixture comprising ATP, TTP, CTP, GTP, recited as being "conventional" nucleotides and dUTP. The method clearly recites that the method results in the reduction of the level of primer aggregates formed during the amplification as compared to amplifying the target nucleic acid using dNTP mix having only conventional nucleotides.

Hence, the method could only be enabled only if dUTP is considered as unconventional. Consistent with the instant specification, the method would only be enabled when the target nucleic acid is DNA, resulting in the nucleotide dUTP being unconventional.

One skilled in the art would not be able to practice the invention in commensurate in scope of the claims without undue experimentation since the method is dependent on the presence and the concentration of the unconventional nucleotide, dUTP, only unconventional when the target nucleic acid is DNA.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 7-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Fraiser et al. (U.S. Patent No. 5,536,649, issued July 16, 1996).

Fraiser et al. disclose a reaction mixture comprising:

a) 0.2 mM of each of dATP, dCTP, dGTP, and dTTP (which is 200 uM); and

b) dUTP (column 5, lines 45-46), anticipating claims 1 and 4.

With regard to claims 2-3, 7, and 8, Fraiser et al. disclose that the concentration of each of dNTP (other than dUTP) will be about 0.1 - 1 mM (or 100 to 1000 uM) and the concentration of dUTP will be about 0.5 - 4 mM (or 500 uM to 4000 uM). Hence, the disclosure disclose a mixture having 1000 uM of dNTPs and 500 uM of dUTP, which results in dUTP not exceeding 75% of the dTTP and having about 50% of the dTTP.

In addition, Fraiser et al. explicitly disclose that, "dUTP is used during amplification (DNA synthesis) at about 0.1-1.0 mM to fully or partially replace TTP...preferably, dUTP fully replaces TTP in the amplification reaction and is included at a higher concentration than each of the other three nucleotides to drive the reaction for maximum substitution..." (column 5, lines 9-15).

With regard to claims 9-11, the reaction mixture of Fraiser et al. comprises Klenow fragment (a polymerase enzyme) (column 7, line 59) and a buffer system (column 7, line 49), employed in an amplification method (column 7, lines 57-67).

With regard to claim 12, the artisans disclose a method of amplifying a target nucleic acid, wherein the method employs a target DNA (*Mycobacterium tuberculosis*) and amplifies said DNA with amplification primers, in the presence of dATP, dCTP, dGTP, and dUTP (column 7, lines 22-33).'

Therefore, invention as claimed is anticipated by Fraiser et al.

Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Monforte et al. (U.S. Patent No. 5,830,655, issued November 3, 1998).

Monforte et al. disclose a mixture comprising a primer pair comprising at least one uracil therein (column 4, line 21 and 55); and a mixture comprising dNTPs. While Monforte et al. is not explicit in the actual concentration employed by the amplification method, it is determined that the requisite concentration is employed as the method of Monforte et al. is also drawn to an amplification reaction.

Therefore, the invention as claimed is anticipated by Monforte et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 6, and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fraiser et al. (U.S. Patent No. 5,536,649, issued July 16, 1996) in view of Haberhausen et al. (U.S. Patent No. 6,248,522 B1, issued June 19, 2001).

Fraiser et al. disclose a reaction mixture comprising:

a) 0.2 mM of each of dATP, dCTP, dGTP, and dTTP (which is 200 uM); and

b) dUTP (column 5, lines 45-46), anticipating claims 1 and 4.

With regard to claims 2-3, Fraiser et al. disclose that the concentration of each of dNTP (other than dUTP) will be about 0.1 - 1 mM (or 100 to 1000 uM) and the concentration of dUTP will be about 0.5 - 4 mM (or 500 uM to 4000 uM). Hence, the disclosure disclose a mixture having 1000 uM of dNTPs and 500 uM of dUTP, which results in dUTP not exceeding 75% of the dTTP and having about 50% of the dTTP.

In addition, Fraiser et al. explicitly disclose that, "dUTP is used during amplification (DNA synthesis) at about 0.1-1.0 mM to fully or partially replace TTP...preferably, dUTP fully replaces TTP in the amplification reaction and is included at a higher concentration than each of the other three nucleotides to drive the reaction for maximum substitution..." (column 5, lines 9-15).

With regard to claims 9-11, the reaction mixture of Fraiser et al. comprises Klenow fragment (a polymerase enzyme) (column 7, line 59) and a buffer system (column 7, line 49), employed in an amplification method (column 7, lines 57-67).

With regard to claim 12, the artisans disclose a method of amplifying a target nucleic acid, wherein the method employs a target DNA (*Mycobacterium tuberculosis*) and amplifies said DNA with amplification primers, in the presence of dATP, dCTP, dGTP, and dUTP (column 7, lines 22-33).

Fraiser et al. do not explicitly teach that a primer should contain a uracil bases therein, or replaces all of the thymidine bases with uracil bases.

Haberhausen et al. disclose a mixture comprising dNTPs, dUTP and primers comprising one or more uracil bases therein, in a method of amplifying a target nucleic acid, said method comprising the steps of amplifying the target nucleic acids with, "U-containing primer," (column 3, line 42), and dNTP mixtures comprising dATP, dCTP, dGTP, and dTTP, and dUTP (column 3, lines 40-44):

"For this dUTP or a U-containing primer is used in the amplification reaction **instead of or in addition to the normal dTTP**…" (column 3, lines 40-44, Haberhausen et al.).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Fraiser et al. and Haberhausen et al., thereby arriving at the claimed invention for the following reasons.

Both Fraiser et al. and Haberhausen et al. employ the uracil base substitute in generating an amplification product from a template DNA, for the purpose of decontaminating products during amplification (column 1, lines 53-55).

Therefore, while Fraiser et al. are not explicitly in stating that the primers themselves should contain uracil bases instead of the thymidine bases, one of ordinary skill in the art at the time the invention was made would have been motivated to also replace the thymidine residues in the primers employed in the amplification process, as evidenced by Haberhausen et al., for the purpose of decontamination during amplification process.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner
Art Unit 1637
9/6/2008

/YJK/